

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
 OF COPIES OF TRANSLATION
 OF THE INTERNATIONAL PRELIMINARY REPORT
 ON PATENTABILITY
 (CHAPTER I OR CHAPTER II
 OF THE PATENT COOPERATION TREATY)
 (PCT Rules 44bis.3(c) and 72.2)

To:

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14. FEB. 2007

Frist:

Date of mailing (*day/month/year*)
 08 February 2007 (08.02.2007)

Applicant's or agent's file reference
 32048P WO

IMPORTANT NOTIFICATION

International application No.
 PCT/EP2005/003460

International filing date (*day/month/year*)
 01 April 2005 (01.04.2005)

Applicant

SINN, Hannsjörg

1. Transmittal of the translation to the applicant.

The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. Transmittal of the copy of the translation to the designated or elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

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The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 32048P WO	FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/EP2005/003460	International filing date (day/month/year) 01.04.2005	Priority date (day/month/year) 02.04.2004	
International Patent Classification (IPC) or national classification and IPC A61K47/48 A61K31/505 A61P37/06			
Applicant ALBUPHARM HEIDELBERG GMBH & CO. KG			

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of _____ sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (<i>sent to the applicant and to the International Bureau</i>) a total of 4 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> <p>4. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application
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Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

This report is based on translations from the original language into the following language _____ which is the language of a translation furnished for the purposes of:

- international search (Rule 12.3 and 23.1(b))
- publication of the international application (Rule 12.4)
- international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):

the international application as originally filed/furnished
 the description:
 pages 1-14 _____ as originally filed/furnished
 pages* _____ received by this Authority on _____
 pages* _____ received by this Authority on _____
 the claims:
 nos. _____ as originally filed/furnished
 nos.* _____ as amended (together with any statement) under Article 19
28.10.2005 with letter
 nos.* 1-20 _____ received by this Authority on of 28.10.2005
 nos.* _____ received by this Authority on _____
 the drawings:
 sheets 1/2, 2/2 _____ as originally filed/furnished
 sheets* _____ received by this Authority on _____
 sheets* _____ received by this Authority on _____
 a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. The amendments have resulted in the cancellation of:

- the description, pages _____
- the claims, nos. _____
- the drawings, sheets/figs _____
- the sequence listing (specify): _____
- any table(s) related to sequence listing (specify): _____

4. This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- the description, pages _____
- the claims, nos. _____
- the drawings, sheets/figs _____
- the sequence listing (specify): _____
- any table(s) related to sequence listing (specify): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims <u>15-20</u>	YES
	Claims <u>1-14</u>	NO
Inventive step (IS)	Claims _____	YES
	Claims <u>15-20</u>	NO
Industrial applicability (IA)	Claims <u>1-20</u>	YES
	Claims _____	NO

2. Citations and explanations (Rule 70.7)

1. Reference is made to the following documents of the search report and the passages cited there:
 - D1: WOLFF DANIEL ET AL: "Methotrexate-albumin and aminopterin-albumin are effective in prophylaxis of experimental acute GVHD." BLOOD, vol. 102, no. 11, 2003, page 404b
 - D2: VALLERA DANIEL A ET AL: "Anti-graft-versus-host disease effect of DT-390-anti-CD3sFv, a single-chain Fv fusion immunotoxin specifically targeting the CD3-epsilon moiety of the T-cell receptor" BLOOD, vol. 88, no. 6, 1996, pages 2342-2353
 - D3: EP-A-0 282 057
 - D4: KRATZ F: "Drug conjugates with albumin and transferrin" EXPERT OPINION ON THERAPEUTIC PATENTS, vol. 12, no. 3, 2002, pages 433-439

- 1.1 Document D1 discloses MTX-HSA and AMPT-HSA for prophylaxis of GVHD.
- 1.2 Document D2 describes the use of a protein-immunotoxin (containing carboxyl groups, organic) conjugate for treatment of GVHD.
- 1.3 Document D3 discloses the use of EDCI for

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement
<p>preparing conjugates of proteins and carboxy compounds such as methotrexate, for example.</p> <p>1.4 Document D4 describes the use of albumin in conjugates for improving pharmacokinetics.</p> <p>2. The present application does not meet the requirements of PCT Article 33(1) because the subject matter of claims 1-14 is not novel under PCT Article 33(2).</p> <p>2.1 Claim 1 relates to the use of an albumin conjugate for modulating a transplantation-associated immune response. Since D1 discloses such a treatment, the subject matter of claim 1 and of dependent claims 2-14 is not novel. The concept used appears to be the same, independently of the method of preparation which produces only different purities.</p> <p>2.2 Claim 15 relates to a method of preparing albumin conjugates using EDCI. In D3, antibody conjugates are prepared, and the subject matter of claims 15-20 is therefore novel.</p> <p>3. The present application does not meet the requirements of PCT Article 33(1) because the subject matter of claims 15-20 does not involve an inventive step under PCT Article 33(3).</p> <p>Claim 15 relates to a method of preparing albumin conjugates using EDCI. D3 which is considered the closest prior art differs in that methotrexate is</p>	

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

coupled to a different protein. However, using this method for coupling methotrexate to albumin rather than to an antibody does not appear to be inventive because this is only one of several obvious possibilities from which a person skilled in the art would choose according to the circumstances in order to solve the problem of interest, without thereby being inventive. The applicant is advised that claim 15 does not define a drug-albumin ratio or rule out the use of N-hydroxysuccinimide. The subject matter of claims 15-20 does therefore not appear to be inventive.